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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,246	01/03/2002	Toshiaki Takezawa	2001-1784A	1296

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,246	TAKEZAWA ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9 and 11-23* is/are pending in the application.

4a) Of the above claim(s) *14-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/11/2005 has been entered.

Claims 1, 3-6, 8, 9 and 11-13 as amended (7/11/2005) are pending and under examination.

Claims 14-23 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected invention(s).

Claim Rejections - 35 USC § 112

Claims 1, 3-6, 8, 9 and 11-13 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 as amended is rendered indefinite by the newly inserted phrase "pre-balanced with a culture medium" because it is uncertain what are final characteristics of the tissue section as intended. The claimed phrase drawn to pre-balancing with culture medium does not point out what is modified and achieved by treatment of tissue with a culture medium. Furthermore it is uncertain whether culture medium is required to be present in the claimed carrier.

In the last response (response 5/11/2005, page 5, par. 4) Applicants indicate that the tissues section is pre-balanced with a culture medium as taught in the Examples. However, the

examples describes several treatment steps for tissues section including embedding, ethanol treatment, washing with salt solution and generic culture medium, staining with hematoxylin-eosin, for example: page 25, par. 1. Thus, the final result of pre-balancing treatment is unclear as claimed and in the light of specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 8, 9 and 11-13 as amended remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,919,624 (Ried et al.) as explained in the prior office action and for the reasons below.

Claims are directed to a tissue section-containing carrier wherein the carrier comprises an animal tissue section with thickness from 0.5 to 50 μm that is attached to a support and "pre-balanced with a culture medium". Some claims are further drawn to the use of various support materials including glass, plastic, etc. Some claims are further drawn to the use of tissue that is fixed, processed for acellularization, embedded. Some claims are directed to the use of tissue derived from mammalians.

US 5,919,624 discloses cervical tissue sections having thickness 4 μm or 8 μm or 50 μm depending on the intended tissue testing (col. 12, lines 5-25). The sections are attached to various support materials including glass or plastic containers. The tissue sections are fixed, paraffin-

embedded and, thus, they are processed for acellularization. The tissue sections are derived from patients or mammalian animals. The limitations drawn to the use of tissues derived from either born or unborn mammals do not provide for any structural and functional differences from the cited tissues that collected from adult patients because the claimed tissue is generic and the age or maturity related differences, if any, cannot be determined. With respect to the newly inserted limitation drawn to pre-balancing with culture medium, it remains uncertain what are final characteristics of tissue section as intended. The cited tissues was stained with the same materials as disclosed in the specification examples and staining procedure is reasonably expected to comprise some washing steps with various reagents including water and salts that are common components of generic culture medium.

Thus, the cited patent is still considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8, 9 and 11-13 as amended remain/are rejected under 35 U.S.C. 103(a) as being obvious over WO 99/12555 (Badylak et al.) and Mori et al. (Anat. Embryol. (1999) 199:319-327) taken with US 5,919,624 (Ried et al.) and US 3,785,234 (Sitte) as explained in the prior office action and for the reasons below.

Claims are directed to a tissue section-containing carrier wherein the carrier comprises an animal tissue section that is 0.5-50 μm thick and that is attached to a support and "pre-balanced with a culture medium". Some claims are further drawn to the use of various support materials including glass, plastic, etc. Some claims are further drawn to the use of tissue that is fixed, treated with reagents or embedded. Some claims are directed to the use of tissue derived from fetal or postnatal mammalian animals.

The reference by Mori et al discloses a tissue section-containing carrier or a tube wherein the tube comprises an animal tissue section that is a preparation of mouse fetal or postnatal liver tissue section. The liver tissue is cut into 240 μm thick slices. The tissue sections are mounted in a plasma clot on cover glass and, thus, attached to the support treated in order to promote tissue adhesion (page 320, col. 1, par. 2) and/or embedded in resin. The liver tissue sections are live and growing. The liver tissue sections are further fixed with methanol and treated with antibody (page 320, col. 2, par. 3).

WO 99/12555 discloses a cell culture carrier or a well plate comprising an animal tissue section such as submucosal tissue attached to a plastic support or holder (example 3, pages 17-18) and that is used for animal cell culture. The tissue section of the cited patent has been demonstrated to support grown of other cells (page 18, at results). The plastic holder is flat in order to keep the tissue flat and thus, it is treated to promote tissue adhesion within the meaning of instant claims. The submucosal tissue is treated with enzyme galastosidase to remove surface epitopes and, thus, to modify tissue microstructure within the meaning of the instant claims. The cited patent teaches that the collection of submucosal tissue preparations includes freezing (page 12, line 29) and also includes treatment with antibodies (page 14, line 4) at least for the purpose

of quality control of the submucosal tissue samples. The submucosal tissue preparations are obtained from mammalian animals (page 4, line 18) and might be 100-200 micrometers (page 4, lines 30-31). Although the cited document does not explicitly indicate whether born or unborn animals were used for tissue collections, it is reasonably to assume that both born and unborn animals have submucosal tissues and, thus, the submucosal tissue preparations used in the cell culture carrier of cited patent meets the meaning of instant claims 12 and/or 13. The submucosal tissue preparations are rinsed with salt solution and treated with a complete cell culture medium (page 18, lines 2-5).

Therefore, the reference by Mori et al discloses that tissue is cut into 240 μm thick slices. WO patent is not particularly clear about thickness of final tissue section that is used as support for culturing cells. However, both preparations are capable to maintain animal cell culture growth regardless their thickness.

The additional references demonstrate that equipment to cut thin tissue sections is available (US 3,785,24 at col.1, lines 10-15) and that thickness of tissue sections is modified accordingly to the intended testing (see US 5,919,624 at col. 12, lines 5-20).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to obtain tissue sections of various thickness with a reasonable expectation of success in culturing animal cells. One of skill in the art would have been motivated to modify thickness of tissue sections with regard to design of culture containers, for example, or with regard to further evaluation of tissue sections as suggested by US 5,919,624 for various testing protocols. One of skill in the art would have been motivated to decrease thickness

of tissue sections for the expected benefits in visual evaluation of tissue section under microscope, for example.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicants' arguments filed 5/11/2005 have been fully considered but they are found not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,919,624 (Ried et al.) applicants argue that the cited paten does not teach tissues section in contact with a culture medium (response 5/11/2005, page 5). However, the claimed invention neither requires the presence of a culture medium nor it is limited by final characteristics resulting from step of pre-balancing the tissue section with a culture medium. Moreover, the claimed culture medium is generic, the culture medium components and function are uncertain as claimed and in the light of specification.

With regard to the claim rejection under 35 USC § 103 applicants' main argument is directed to the idea that the combined teaching of the cited references would not motivate ordinary skill in the art to prepare a tissue section accordingly to the claimed invention including the use of thickness 0.5-50 μm (response 5/11/2005, page 6). This argument is not found persuasive because prior art demonstrates culturing cells on tissue sections of various thickness

and the methods of cutting tissues into sections of various thickness including 0.5-50 μm are known in the prior art. One of skill in the art would have been motivated to modify thickness of tissue sections with regard to a particular design of a culture container, for example, or with regard to further evaluation of tissue sections as suggested by US 5,919,624 for various testing protocols. One of skill in the art would have been motivated to decrease thickness of tissue sections for the expected benefits in visual evaluation of tissue section under microscope, for example. Most importantly, the criticality of tissue section being 0.5-50 μm thick is uncertain as argued and as disclosed. Moreover, the resin-embedded and frozen tissue sections are cut into slices 0.5-50 μm thick as disclosed (page 24, for example). The final thickness of tissue section for seeding and culturing cells is unknown as disclosed. For example: it is uncertain whether washing or pre-balancing sliced tissue section with solution and/or culture medium would not modify its thickness. The washed and/or "pre-balanced" tissue sections could be swollen and, thus, their thickness would be greater than original 0.5-50 μm thickness. Therefore, there would not be any structural differences that appear to be argued. Moreover, the claimed tissue is generic and, thus, functional differences, if any, remain undetermined as claimed and as argued.

Therefore, applicants' arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Applicants' arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

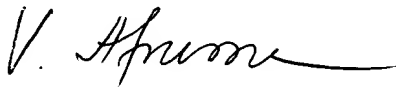
The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

September 2, 2005



VERA AFREMOVA

PRIMARY EXAMINER